UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,177	01/23/2004	Mark Tengler	NEOS:1007	7865

34725 7590 02/22/2008

CHALKER FLORES, LLP
2711 LBJ FRWY
Suite 1036
DALLAS, TX 75234

EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
02/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,177	TENGLER ET AL.	
	Examiner	Art Unit	
	JAMES D. ANDERSON	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,8-21,25-43 and 45-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,6,8-21,25-43 and 45-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 6, 8-21, 25-43, and 45-61 are presented for examination

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/3/2007 has been entered.

Status of the Claims

Applicants' amendment filed 12/3/2007 has been received and entered into the application. Accordingly, claims 1, 20, 60, and 61 have been amended.

Applicants' arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Arguments

Applicant's arguments filed 12/3/2007 have been fully considered but they are not persuasive. Applicants assert that the combination of references fail to teach every element of the present invention.

In this regard, Applicants argue that the combination of Devane *et al.* and Dang *et al.* do not teach an enveloped composition having a first active available for immediate release, wherein over 80% of the first active disposed on a carrier and is released within 60 minutes and a second active is disposed on a bead for extended release and an extended release coating wherein the second active includes three or more layers of the second active agent and wherein over 80% of the second active is released between 90 minutes and 6 hours. However, contrary to Applicants' assertion, Devane *et al.* provide a multi-particulate modified release composition in which a first portion of the active ingredient is released immediately upon administration and a second portion is released rapidly after an initial delay period (*i.e.* extended release) in a bimodal manner (col. 3, lines 51-56). The first and second components are disposed on separate carriers (*i.e.* particles) (col. 4, lines 10-14) and can be the same or different (col. 4, lines 14-16). The active ingredient-containing particles of the second component are coated with a modified release coating (col. 4, lines 15-18). Devane *et al.* further teach that by modifying the excipients or coatings of the particles, the time-release characteristics of the active ingredient from each component may be varied (col. 7, lines 38-42). Dang *et al.* provide the motivation to combine the claimed active agents into a single composition wherein they teach that compositions comprising guaifenesin and phenylephrine, provide the immediate expectorant action of guaifenesin and the prolonged decongestant action of phenylephrine (col. 2, lines 11-13) and that such a combination produces a composition possessing "sympathomimetic decongestant and expectorant properties superior to the use of either one of the compounds alone" (col. 1, line 65 to col. 2, line 3). The cited references thus provide clear motivation to combine guaifenesin and

phenylephrine in a single composition and further provide the means to formulate a combination having a first active for immediate release and a second active for extended release.

Applicants further argue that the combination of references does not teach the active agents being on separate carriers, that the combination of references does not teach the use of an extended release coating and an extended release matrix (*i.e.*, bead), and that the combination of references does not teach the addition of three or more layers on the second active agent. However, Devane *et al.* and Davis *et al.* both teach combinations of immediate release and extended release active agents disposed on separate carriers. The formulations of Davis *et al.* relate to sustained release preparations in the form of capsules having beads or granules of both immediate release formulation and beads or granules of sustained release formulation (page 2, ¶ [0019]). With respect to the claimed "three or more layers of the second active agent", it is well within the purview of the skilled artisan to modify the amounts of active agents present in the compositions disclosed in the cited prior art. This is especially true given the fact that the references suggest that excipients, coatings, etc. can all be modified in order to elicit modified release profiles.

The 35 U.S.C. 103 rejection of claims 1, 6, 8-21, 25-43, and 45-61 is maintained for the reasons of record and reiterated below.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6, 8-21, 25-43, and 45-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

Regarding the requirement for adequate written description of chemical entities, Applicant's attention is directed to the MPEP §2163. In particular, *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1568 (Fed. Cir. 1997), *cert. denied*, 523 U.S. 1089, 118 S. Ct. 1548 (1998), holds that an adequate written description requires a precise definition, such as by structure, formula, chemical name, or physical properties, "not a mere wish or plain for obtaining the claimed chemical invention." *Eli Lilly*, 119 F.3d at 1566. The Federal Circuit has adopted the standard set forth in the Patent and Trademark Office ("PTO") Guidelines for Examination of Patent Applications under the 35 U.S.C. 112.I "Written Description" Requirement ("Guidelines"), 66 Fed. Reg. 1099 (Jan. 5, 2001), which state that the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics," including, *inter alia*, "functional characteristics when coupled with a known or disclosed correlation between function and structure..." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 316, 1324-25 (Fed. Cir. 2002) (quoting *Guidelines*, 66 Fed. Reg. at 1106 (emphasis added)). Moreover, although *Eli Lilly* and *Enzo* were decided within the factual context of DNA sequences, this does not preclude extending the reasoning of those cases to chemical structures in general. *Univ. of Rochester v. G.D. Searle & Co.*, 249 Supp. 2d 216, 225 (W.D.N.Y. 2003).

In the instant case, the claims are replete with functional language that fails to define what the claimed pharmaceutical compositions are made of. Examples of such functional language include the following:

i) "....enveloped pharmaceutical composition...";

ii) "...a first active available for immediate release, wherein over 80% of the first active is released within 60 minutes...";

iii) "...wherein the first active is disposed on a carriers [*sic* – carrier]...";

iv) "....and the second active is disposed on a bead...";

v) "a second active for extended release....and an extended release coating...and wherein over 80% of the second active is released between 90 minutes and 6 hours".

In the above examples, there is no description of what the composition is enveloped in, what excipients allow for the claimed release profile of the first active agent, what the carrier is composed of, what the beads are composed of, or what extended release excipients allow for the claimed release profile of second active agent. As such, the claims lack written description because the claimed pharmaceutical compositions are not adequately described in a manner that would indicate what the compositions are composed of.

The lack of written description of the instantly claimed compositions is further compounded by the fact that the compositions require specific release profiles of the first and second active agents. Accordingly, other than the specific formulations described in the examples (pages 23-25), Applicants have not described the enveloping materials, excipients, carriers, or extended release coatings that would result in the claimed first and second active agent release profiles.

Aside from the very limited examples provided in the specification, Applicants provide no direction as to (a) what excipients and extended release coatings out of all possible excipients and release coatings that exist in the art would have been reasonably expected to result in the claimed release profiles and (b) which of those excipients and extended release coatings actually *do* result in the claimed release profiles without having to execute hit or miss testing practices in order to make such a determination.

The need for testing amongst varying species and amounts of excipients and release coatings to determine what combinations would result in the claimed release profiles demonstrates that Applicants were not in possession of the full scope of the compositions now presently claimed. "Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention." Please see MPEP § 2163.

Despite the disclosure of specific in-actives, substrates, solubilizers, and other additives, *e.g.*, pages 17-23 of the specification, it remains that the claims recite a solely functional pharmaceutical composition. With the exception of the specific formulations described in the examples, Applicants are imposing the burden of extensive testing upon the skilled artisan to identify those other excipients, carriers, in-actives, and extended release coatings that may result in the claimed release profiles of the first and second active agents, but which Applicants have not identified and thus, were not in possession of, at the time of the present invention.

It has been held in patent law that a wish or plan for obtaining the invention as claimed does not provide adequate written description of a chemical invention. Rather, a precise definition, such as by structure, formula, chemical name or physical properties or a combination thereof, is required. Please reference, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004). In other words, though Applicants may have a plan for how to identify other excipients, carriers, in-actives, and extended release coatings that may be amenable for use in the present invention, it remains that at the time of the invention, Applicants had not identified such excipients, carriers, in-actives, and extended release coatings, and, therefore, did not have written description of the full scope of the compositions now claimed.

Further, though Applicants have limited the claimed compositions to those that have particular release profiles of active agents, it remains that Applicants have not appropriately defined the metes and bounds of the claimed compositions, even when limited by function (step-plus-function form). As taught in the MPEP at § 2163, step-plus-function claims are not adequately described if "the written description adequately links or associates adequately described particular structure, material or acts to the function recited in a step-plus-function claim limitation," or if "it is clear based on the facts of the application that one skilled in the art would have known what structure, material, or acts perform the function recited in a step-plus-function limitation." The instant application fails to meet these criteria. The present specification provides no disclosure beyond the generic disclosure of the required function that would correlate a common structural element or material to performance of the claimed function and that would be readily identifiable to one of skill in the art.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 6, 8-21, 25-43, and 45-61 are again rejected under 35 U.S.C. § 103(a) as being unpatentable over **Devane *et al.*** (U.S. Patent No. 6,228,398; Issued May 8, 2001) in view of **Dang *et al.*** (U.S. Patent No. 6,462,094; Issued Oct. 8, 2002) (cited by applicants) and **Davis *et al.*** (US 2003/0049318 A1; Published Mar. 13, 2003) (prior art of record).[1]

[1] Devane *et al.* qualifies as prior art under 35 U.S.C. § 102(b). Dang *et al.* and Davis *et al.* qualify as prior art under 25 U.S.C. § 102(a) and 102(e).

The instant claims are drawn to enveloped pharmaceutical compositions comprising a first active for immediate release and a second active for extended release wherein the first active is disposed on a carrier and the second active is disposed on a bead (*e.g.* Claim 1). Applicants state that the problem to be solved in the prior art at page 4, ¶ [0013]:

> "It has been found, however, that the present methods fail to provide an efficacious amount of a first active ingredient in an immediate release form and a second active that is provided as an extended release formulation that takes advantage of the pharmacological effect of the immediate release active to maximize the efficiency of the delivery and pharmacological action of the second active. Yet another problem is that certain drugs affect the release profile of a second drug that is being provided in a single dose. The present invention solves these problems in the art."

To solve the prior art problems as presented in the instant case, one skilled in the art would need the means to formulate an enveloped composition comprising a first active for immediate release and a second active for extended release (wherein the first and second actives are provided on separate carriers). The skilled artisan would also need a motivation to formulate such a composition with guaifenesin and phenylephrine. Examiner herein presents a *prima facie* case of why the instantly claimed compositions would have been obvious to one of ordinary skill in the art.

Devane *et al.* disclose multi-particulate modified release compositions that deliver active ingredients in a pulsed or bimodal manner (Abstract). One object of the invention is to provide a multi-particulate modified release composition in which a first portion of the active ingredient is released immediately upon administration and a second portion is released rapidly after an initial delay period (*i.e.* extended release) in a bimodal manner (col. 3, lines 51-56). The first and second components are disposed on separate carriers (*i.e.* particles) (col. 4, lines 10-14) and can

be the same or different (col. 4, lines 14-16). The active ingredient-containing particles of the second component are coated with a modified release coating (col. 4, lines 15-18). In a preferred embodiment, the first component is an immediate release component (col. 4, lines 24-26). The patentees further contemplate combined therapy. For example, when the first and second components are different, an enhancer compound or a sensitizer compound in another component of the composition may accompany the drug compound present in one component in order to modify the bioavailability or therapeutic effect of the drug compound (col. 6, line 64 to col. 7, line 8). **By modifying the excipients or coatings of the particles, the time-release characteristics of the active ingredient from each component may be varied** (col. 7, lines 38-42). The invention of Devane *et al.* is exemplified in a preferred embodiment as recited at col. 8, lines 22-29) (emphasis added):

> In a preferred embodiment, the multi-particulate modified release composition according to the present invention has an immediate release component and at least one modified release component, the immediate release component comprising a first population of active ingredient containing particles and the modified release components comprising second and subsequent populations of active ingredient containing particles.

The reference thus teaches first and second actives that are different being composed on separate carriers. The multi-particle modified release composition according to the reference may be incorporated into any suitable dosage form, including filling into capsules, such as hard or soft gelatin capsules or compressed into mini-tabs and subsequently filled into capsules (col. 10, lines 15-27), thus teaching an "enveloped" composition. The compositions taught in the reference can also include one or more inactives as recited in instant claims 18, 38, and 58 (Table 2). The

reference also discloses the instantly claimed dissolution rates recited in claims 6, 8, 25-27, 40 and 46-48 (col. 12, lines 15-21 and Table 3).

Thus, while Devane *et al.* provide the means to formulate an enveloped composition of a first active for immediate release and a second active for extended release, they do not teach that the first active comprises guaifenesin or that the second active comprises phenylephrine. Devane *et al.* also do not teach that the second active is selected from the group consisting of a decongestant, an antihistamine, an expectorant, or an antitussive.

However, Dang *et al.* is provided as evidence that combined guaifenesin and phenylephrine compositions were known in the art at the time the present invention was made. The patentees disclose that guaifenesin has an expectorant action, which increases the output of respiratory tract fluid by reducing adhesiveness and surface tension (col. 2, lines 3-5). The compositions described in Dang *et al.*, comprising guaifenesin and phenylephrine, provide the immediate expectorant action of guaifenesin and the prolonged decongestant action of phenylephrine (col. 2, lines 11-13). The compositions may be prepared for oral administration in the form of powders, capsules, elixirs, syrups and the preferred forms of tablets or suspensions (col. 2, lines 15-17). The reference thus provides one skilled in the art with the motivation to formulate a composition comprising guaifenesin and phenylephrine wherein the patentees state that the combination produces a composition possessing "sympathornimetic decongestant and expectorant properties superior to the use of either one of the compounds alone" (col. 1, line 65 to col. 2, line 3). Dang et al. differ from the instant claims in that they do not teach a composition comprising guaifenesin available for immediate release and a decongestant (e.g., phenylephrine) available for extended release.

However, Davis *et al.* disclose immediate and sustained release formulations of guaifenesin and additional drug ingredients, including antitussives (*e.g.* codeine) and decongestants (*e.g.* phenylephrine) (Abstract; page 4, ¶ [0045]). Said formulations relate to sustained release preparations in the form of capsules having beads or granules of both immediate release formulation and beads or granules of sustained release formulation, thus teaching or suggesting the limitations of claims 1, 9, 12-15, 19-21, 28-30, 32-35, 37, 39-43, 49-50, 52-55, 57, and 59-61 (page 2, ¶ [0019]). Davis *et al.* explicitly contemplate capsules (*i.e.* enveloped composition) having a combination of "beads or granules of immediate release formulation and beads or granules of sustained release formulation" (*i.e.* disposed in separate carriers) (page 4, ¶ [0043]). They go on to state that the invention will be described in detail in the context of the bi-layer tablet embodiment (*id.*). "Granules" (page 4, ¶ [0043]) of immediate release guaifenesin read on guaifenesin "in a powder form" as instantly claimed *(e.g.* claim 10). The formulations of the invention can also include other excipients (page 4, ¶ [0050]), thus teaching the limitations of claims 18 and 38. The reference thus motivates and suggests capsules containing both immediate release and sustained release formulations that can reasonably contain guaifenesin and phenylephrine.

The cited prior art discloses compositions comprising guaifenesin and phenylephrine, both in immediate release and immediate/sustained release formulations. The cited prior art also provides methods for formulating drug compositions comprising immediate release granules or beads and sustained released beads in an enveloped composition having the dissolution profiles instantly claimed. The prior art differs from the instant claims in that no single reference discloses enveloped compositions comprising an immediate release agent (*e.g.* guaifenesin) and

a sustained release agent that is a decongestant (*e.g.* phenylephrine) disposed on separate carriers having the dissolution profiles instantly claimed. The level of ordinary skill in the art is that of an M.D., Ph.D. or pharmacist.

However, in the absence of a showing of unexpected results commensurate in scope with the claims, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the multi-particle modified release compositions disclosed in Devane *et al.* and Davis *et al.* by providing immediate release guaifenesin and extended release phenylephrine particles. Dang *et al.* and Davis *et al.* both provide the motivation to do so. Dang *et al.* disclose that combined guaifenesin/phenylephrine compositions provide immediate decongestant action of guaifenesin and extended expectorant action of phenylephrine. Davis *et al.* disclose compositions comprising immediate release guaifenesin and sustained release guaifenesin with additional drug ingredients, including the instantly claimed antitussives and decongestants (*e.g.* phenylephrine). Although Davis *et al.* exemplify bi-layer tablet formulations, capsules containing immediate release and sustained release beads are also disclosed. It is noted that the dissolution profiles disclosed in Davis *et al.* for sustained release formulations are longer than those instantly claimed. However, it well within the level of ordinary skill in the art to modify release profiles of drugs by changing the sustained release layer as evidenced by Devane *et al.*

Thus, one skilled in the art had the means (Devane *et al.* and Davis *et al.*) and the motivation (Dang *et al.* and Davis *et al.*) to formulate an enveloped composition comprising an immediate release first active and a sustained release second active wherein the first and second actives are disposed on separate carriers and the first active is guaifenesin and the second active

is phenylephrine. Applicants have provided no evidence of unexpected results with the instantly claimed compositions of guaifenesin and phenylephrine.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JAMES D. ANDERSON whose telephone number is (571)272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/James D Anderson/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614